

### Non-elected Claims

Non-elected claims 1-6, 19, 21 and 23-26 are canceled without prejudice to applicants right to claim the same in one or more divisional applications.

### Amendments to the Claims

Claim 7 is amended to cancel "or modified form" as superfluous since "a purine or pyrimidine" clearly includes conventional purines or pyrimidine analogs such as discussed, for example, on page 5, lines 17-20. The claim is also amended to exclude known 5'-methylene phosphonates.

Claims 10 and 14 are amended to more clearly depend on claim 7 and to provide antecedent basis for claims 11-13 and 15-18. New claims 27 and 28 recite the guanine language originally present in claims 10 and 14.

Claim 20 is amended to read in independent form while incorporating the language of original claim 7.

New claims 29-42 describe other embodiments of the invention. Support for the definition of B in claims 29 and 33 is at the bottom of Table 1 on page 8. Support for the definition of B in claims 30-32 and 34 is found at page 5, line 36 to page 6, line 2. Claim 35 describes pharmaceutical compositions of the compounds of claim 29. Claims 36 and 37 describe pharmaceutical compositions of the compounds 34-40 of Table 3 on page 10 and the compounds 76-82 in Table 6 on page 13. Claim 38 describes the compounds in which X is S. Claim 39 describes the compounds in which Y is O alkyl. Claim 40 describes compounds which are 3-OH and 2-H or 2-OH. Claim 41 describes compounds of substituted bases in Table 1 on page 8 and claim 42 describes compounds of protected bases found at page 5, line 36 to page 6, line 2.

No new matter is introduced by these amendments.

### 35 USC §102(b)

Claim 7 was rejected under 35 USC §102(b) as anticipated by Padyukova et al.

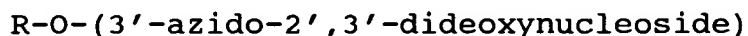
This claim is amended to exclude the two compounds disclosed in Padyukova et al. Accordingly, claim 7 is not anticipated. Reconsideration and withdrawal of the rejection are respectfully requested.

35 USC §103

I. Claims 8-9, 11-12, 14-16 and 18 were rejected under 35 USC §103 as obvious over Robins et al. or Balzarini et al. or Ranganathan or Martin et al. in view of Khorlin et al.

Robins et al., Balzarini et al., Martin et al. and Ranganathan disclose certain nucleosides. There is no teaching or suggestion to make any phosphonate derivatives of these nucleosides, much less methylene phosphonates.

Khorlin et al. discloses 5'-phosphonates of 3'-azido-2',3'-dideoxynucleosides. However, these phosphonates all have the structure



where R is  $-PH(O)OH$ ,  $-CH_2P(O)(OH)_2$  or  $P(O)CH_3OH$ .

By contrast, the compounds of the claims are characterized by the absence of any oxygen between the nucleoside and the R phosphonate group.

Thus, the combined teaching of the art points away from the invention by always requiring an oxygen linkage between the nucleoside and the phosphonate while the compounds of the claims require a methylene linkage and no oxygen.

In view of the above, the claims are not obvious, much less prima facie obvious, from the combined teaching of the art relied upon by the Examiner. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

II. Claims 20 and 23 were rejected under 35 USC §103 as being obvious over Padyukova et al.

In view of the amending of claim 20 as described above, the claims do not contemplate formulation of a known

antiviral agent with a pharmaceutical carrier. Padyukova et al. does disclose a methylene phosphonate but there is no teaching or suggestion that such compounds have antiviral activity.

Accordingly, the claims are unobvious in view of Padyukova et al. Reconsideration and withdrawal of the rejection are respectfully requested.

35 USC §112, First Paragraph

The specification was objected to and claims 7-18, 20 and 22 were rejected under 35 USC §112, first paragraph, as failing to provide an enabling disclosure.

It is well recognized that examples are not required as a prerequisite for enablement (In re Borkowski, 164 U.S.P.Q. 642). It is the specification itself which must be enabling to those of skill in the art with adequate guidance of how to use the compounds.

The specification describes to those of skill in the art how to use the compounds as antiviral and antitumor agents as well as their use as intermediates to oligonucleotides having diagnostic and therapeutic applications such as at pages 4-7 of the specification. Such use is not incredulous since a variety of nucleotides and oligonucleotides are known in the art such as PCT WO84/04748 (cited by Applicants 6/21/91) describing acyclic methylene phosphonates to have such properties, and a variety of nucleotides are known as intermediates to oligonucleotides having intrinsic value.

There is no evidence in the record to cast doubt on Applicants' teachings. On the contrary, Applicants' teachings are consistent with the general knowledge of the art to other nucleotides and oligonucleotides.

Reconsideration and withdrawal of the rejection are respectfully requested.

### 35 USC §112, Second Paragraph

Claims 7 and 11-13 were rejected under 35 USC §112, second paragraph, as indefinite.

Claim 7 is amended to cancel "or modified form" as it is clear from the specification, e.g., page 5, lines 17-20, the examples and elsewhere, that "a purine or a pyrimidine base" includes conventional analogs.

Applicant does not understand the Examiner's reference to both R<sup>1</sup>s since the wording states that each can be chosen independently in the same manner that Y and R<sup>2</sup> can be chosen independently. In the event that the Examiner is referring to the wavy lines connecting R<sup>1</sup> to the ring, such lines are conventional nomenclature indicating that each R<sup>1</sup> can be either up or down with regard to the plane of the ring.

Claims 10 and 14 are amended to provide antecedent basis for the subsequent dependent claims. It is believed clear from the specification, claims 11-13 and 15-18 and Table 6, that B with reference to formulas V and VI includes purine and pyrimidine bases besides just guanine. New claims 27 and 28 are added specific to B as guanine.

In view of the above, the claims are definite to those of skill in the art. Reconsideration and withdrawal of the rejection are respectfully requested.

### Information Disclosure Statement

(1) Applicant resubmits a copy of the Information Disclosure Statement (IDS) originally submitted June 12, 1991. Copies of each document listed are also submitted. Since both the original IDS page 1 and the post card receipt state that copies of the references were sent, the copies were apparently inadvertently misplaced by the Office and no fee is due for resupplying them.

(2) Also, Applicant submitted three Supplemental Information Disclosure Statements on March 13, 1992, July 7, 1992, and March 19, 1993, would appreciate the Examiner

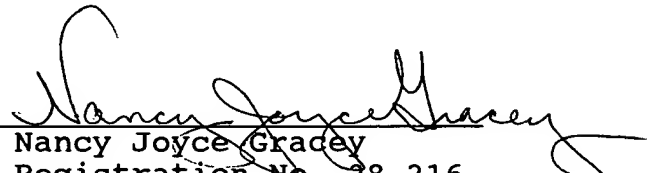
returning a copy of each Form-1449 initialed by the Examiner.

Summary

This application is in condition for allowance, which allowance is now respectfully requested. If the Examiner has a question about this response or would like to discuss the status of this application, the Examiner is requested to telephone the undersigned at the telephone number given below.

Respectfully submitted,

By:

  
Nancy Joyce Grady  
Registration No. 28,216

Morrison & Foerster  
755 Page Mill Road  
Palo Alto, CA 94304-1018  
Telephone: (415) 677-6332  
Fax: (415) 677-7522

Enclosures: Copy of IDS of 6/12/91 and documents listed thereon.



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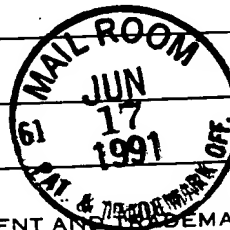
DATE 12 June 1991

PAPER: Information Disclosure Statement, Form PTO-1449s,  
Copies of references

INVENTOR: Chris Buhr et al.

SERIAL NO.: 07/052,970

FILING DATE: 8 February 1991



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